Allergy Abstracts

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The Jewish Hospital of Brooklyn

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Asthma and Hay Fever

A Clinical Study of Prednisone in Severe Intractable Bronchial Asthma. Jenkins, C. M.: Ann. Allergy **13**: 700, 1955.

Thirteen patients, ranging in age from 18 to 68 years and suffering from perennial bronchial asthma of at least 2 years' duration, were treated with Prednisone. The usual antiasthmatic measures had failed to benefit these patients. In each case, ACTH, cortisone, and hydrocortisone had suppressed the asthmatic symptoms, but had produced objectionable side effects, the most frequent being sodium and fluid retention. Prior to the administration of the Prednisone, blood counts, blood pressures, vital capacities, fasting blood sugars, serum sodium and potassium levels were computed.

The patients were placed on a normal diet without sodium restriction or added potassium. Initial dosage of Prednisone was 40 mg. per day (10 mg. every 6 hours) for the first day, and 30 mg. per day (7.5 mg. every 6 hours) for 2 days or until complete suppression of symptoms was apparent. Thereafter dosage was reduced by 5 mg. every 4 days until a maintenance level was established. This was usually 10 mg. per day, but ranged as high as 20 mg. per day in one case. Marked clinical improvement was usually experienced after 12 to 48 hours and continued for the 11 to 15 weeks during which the group was treated.

Results of the laboratory studies made before and after institution of the therapy revealed the following: (1) there was often an initial weight loss which was believed to be due to the elimination of previously retained sodium and fluid; 2 of 3 patients who had developed moon face while under

treatment with other steroids improved after 8 weeks of Prednisone therapy; (2) serum sodium and potassium were at normal levels after 4 weeks of therapy and there was no clinical evidence or EKG signs of potassium deficiency; (3) fasting blood sugars were within normal limits and no glycosuria was observed; (4) blood pressure readings never became elevated and in 10 patients dropped; (5) vital capacities were increased up to 2,100 c.c.; (6) the 17-ketosteroid levels in the urine were suppressed and the absolute eosinophile counts were markedly reduced.

Two patients complained of epigastric distress and burning which was relieved by aluminum hydroxide gel and one patient showed some evidence of demineralization of the third lumbar vertebra. Mild insomnia, perspiration of the hands, and increased appetites were other minor side effects. H. F.

First Clinical Trials With Prednisone (Metacortandracin or Meticorten). Bickel, G.: Schweiz. med. Wchnschr. **85**: 895, 1955 (Abstract, J. A. M. A. **159**: 1249, 1955.

As a therapeutic trial, Prednisone was given to a group of 13 patients, which included 3 cases of bronchial asthma. Two of the asthmatics were given 20 mg. of Prednisone daily instead of their usual dose of 80 to 100 mg. of cortisone. The third asthmatic who was not on cortisone therapy was given 60 mg. of Prednisone for 2 days, 40 mg. for 4 days, and then 20 mg. daily thereafter. The effective results which were obtained in these 3 patients indicated that Prednisone was superior to cortisone and hydrocortisone as an antiallergic drug. In the entire series, less pronounced and less frequent side effects occurred with Prednisone than with the other steroids. However, gastralgia developed in 4 cases, and in another case a sudden bout of hematemesis occurred. The marked initial beneficial effects of the drug were found to diminish gradually in some patients as treatment was continued. This necessitated increasing the dose of the drug. M. C.

Treatment of Asthma by Corticotherapy: Based on Ninety-five Cases. Vallery-Radot, P., Laroche, C., and Lyon, G.: Presse méd. **63**: 1043, 1955 (Abstract, J. A. M. A. **159**: 711, 1955).

ACTH, cortisone, and hydrocortisone were used to treat 95 patients with severe bronchial asthma. There were 15 patients who failed to respond to this form of therapy, 4 of whom died. The usual lesions of status asthmaticus were found on post-mortem examination. Long-term steroid therapy was given to 16 patients, some of whom were treated for 3 years. Results were good in 12 patients, fair in one patient, and poor in 3. It was not possible to determine in advance which patients would respond favorably to steroid therapy. M. C.

Clinical and Physiological Studies on the Use of Metacortandracin in Respiratory Disease. I. Bronchial Asthma. Barach, A. L., Bickerman, H. A., and Beck, G. J.: Dis. Chest. **27**: 515, 1955.

Metacortandracin (Prednisone) was administered in doses of 40 to 80 mg. a day to patients with chronic, severe, bronchial asthma. These patients, whose ages ranged from 14 to 72 years of age, received larger doses for the first two or three days, after which the amount of drug administered was gradually reduced to a maintenance dose of 30 to 40 mg. per day. Eighteen of the 30 patients in this series had been previously treated with cortisone, hydrocortisone, or ACTH. The relief afforded by metacortandracin was more rapid than that observed with other steroids. Subjective benefit occurred

within 24 to 48 hours in 25 of the 30 cases, and 17 had complete remissions. Twelve, or 40 per cent, had partial remissions and were classified as being moderately benefited. One patient who had been hospitalized for 12 years, and who was addicted to Demerol, experienced no benefit from treatment with metacortandracin. Ventilatory function tests performed on 21 patients four to seven days after the beginning of metacortandracin therapy revealed a marked improvement in vital capacity and in the fast expiratory volume. The mean per cent change in the vital capacity was 53.2 per cent and in the fast expiration 63.6 per cent. The maximal breathing capacity after metacortandracin revealed a mean change of 44.5 per cent in the 8 patients tested. Side effects encountered in treatment with this drug included reddening of the palmar surface of the hand in one case, headache in 3 patients, dizziness in 3 patients, recurrence of undue stimulation in one patient, and abdominal distress in 3 patients. Metacortandracin was also found to be superior to other steroids in that its use did not require limitation of salt intake. It was also noted that in patients who had previously been treated with other steroids the moon shape of the face and the weight gain disappeared under metacortandracin therapy. The authors feel that metacortandracin is a drug of considerable value in the treatment of intractable bronchial asthma. E. W.

Bronchial Asthma Caused by Pseudomonas Aeruginosa Diagnosed by Bronchoscopic Examination. Fein, B.: Ann. Allergy **13**: 639, 1955.

A 7-year-old female with a positive family history of allergy developed wheezing respirations which, for short periods of time, responded to antibiotic therapy. There was a history of exposure to feathers and dog dander, dating from the time of onset of wheezing. Skin tests revealed positive reactions to house dust, mesquite, and mountain cedar. Nasal and sputum smears were negative for eosinophiles. X-ray failed to reveal any obstructing foreign body. After antiallergic management had failed to provide relief from symptoms, the child was bronchoscoped. Smears taken at this time and subsequent cultures revealed the presence of the ordinarily nonpathogenic Pseudomonas aeruginosa. This organism had not been found on previous sputum cultures. Treatment with polymixin B, to which the organism was demonstrated to be highly sensitive, resulted in complete relief in symptoms. H. F.

Dermatology

Fixed Eruption. Cornbleet, T., Hoit, L., and Sickley, J. F.: Arch. Dermat. **71**: 507, 1955.

The authors studied the incidence of phenolphthalein sensitivity in patients hospitalized over a 25-year period from 1928 to 1953. There were 1,600,000 admissions during this time, of which about 5,000 patients were admitted to the dermatologic service during the last 13 years of the study. In the period from 1928 to 1939, only one of the two suspected cases was proved to have had a phenolphthalein eruption. Among the charts reviewed in the last 14 years of the survey when patients were hospitalized on the dermatologic service, there were 8 suspected, though unverified, cases of phenolphthalein reactions. Combining the clinic and hospital patients with suspected phenolphthalein eruptions, there were 18 individuals available for further study. They were each given 300 mg. of antipyrine followed in 48 hours by 90 mg. of phenolphthalein. If a reaction occurred from the first medication, the second drug was withheld until the reaction had subsided.

Four fixed drug responses were observed. Three occurred from the phenolphthalein, and one from the antipyrine. Two patients developed an

erythema multiforme-like eruption from antipyrine. Two unclassified eruptions followed the ingestion of phenolphthalein. In 10 of the 18 patients, there were no allergic responses to either drug. There was no evidence of cross sensitivity between antipyrine and phenolphthalein. Although phenolphthalein is commonly ingested by a vast number of people, the authors emphasize that this drug has been highly overrated as an important cause of dermatologic reactions, especially those of the fixed eruption type. R. W.

Crossed Fixed Drug Eruption From Three Antibiotics. Welsh, A. L.: Arch. Dermat. **71**: 521, 1955.

A patient who had a previous fixed drug eruption from chlortetracycline (Aureomycin) and a crossed fixed drug eruption from oxytetracycline (Terramycin) was given two 5 Gm. courses of tetracycline (Achromycin, Tetracyn, Polycyline) six months following his first course of tetracycline. Within one hour, severe pruritus occurred at all the sites of his previous eruption. The areas were easily discernible because of the residual pigment still present. Urticaria, erythema, and bullous lesions developed and the itching became generalized. No lesions were noted except in the areas of the previous rash. The pruritus subsided in two days; the lesions faded in five days. Pigmentation at the fixed eruption sites, which had become more pronounced after the flare-up from oxytetracycline, became even more intense following the reaction from the tetracycline. Since the tetracycline ring is common to all three of these antibiotics, the author concludes that this factor is the cause of the crossed fixed drug eruption. He further emphasizes the fact that fixed drug eruptions due to chlortetracycline may be reactivated by oxytetracycline and also by tetracycline. R. W.

Use of Hydrocortisone and 9-alpha-fluorohydrocortisone Derivatives. Evaluation in The Treatment of The Pruritic Dermatoses. Lubowe, I. I.: Arch. Dermat. **72**: 164, 1955.

Hydrocortisone was incorporated into a shake lotion consisting of isopropyl alcohol, oil, and an emulsified aqueous base. The suspension was dispensed in a squeeze bottle to improve its cosmetic acceptability and to make it easier to apply topically with a minimum of waste. The lotion was employed in treating 49 patients with various dermatoses for a period of 9 months. Excellent results were obtained in atopic dermatitis and in contact dermatitis. No evidence of eczematous sensitization was observed. The liquid was just as effective as 1 per cent hydrocortisone ointment and produced almost immediate relief because of its rapid penetration.

The clinical effectiveness of 9-alpha-fluorohydrocortisone lotion and ointment in concentrations of 0.1 per cent and 0.25 per cent was studied in 132 patients suffering from all types of dermatitis. The preparations were rubbed into the skin 3 times daily. The 0.1 per cent preparation was found to be as effective as 1 per cent hydrocortisone ointment in relieving itching and improving atopic dermatitis. The 0.25 per cent preparations compared favorably with the 2.5 per cent hydrocortisone ointment in relieving the pruritus and lessening the lichenification of neurodermatitis. Upon discontinuance of the inunctions, patients often experienced a return of symptoms, but this could be prevented in most cases by a single daily application. The ointment base appeared to be slightly superior to the lotion, probably because of its additional emollient effect. Several patients used the preparations for many months with no evidence of constitutional symptoms which would indicate that there had been absorption of topical hydrocortisone. The 9-

alpha-fluorohydrocortisone caused no uncomfortable local reactions and has a low incidence of sensitization. The author believes that topical preparations of 9-alpha-fluorohydrocortisone are clinically effective in significantly lower concentrations than hydrocortisone. R. W.

Evaluation of 9-α-fluorohydrocortisone Acetate in the Treatment of Various Inflammatory Dermatoses. Wright, E. T., Graham, J. H., Newcomer, V. D., and Sternberg, T. H.: Arch. Dermat. **72**: 69, 1955.

The authors studied the effect of 9-α-fluorohydrocortisone in the treatment of 64 patients with various inflammatory dermatoses. Eight of the group had atopic dermatitis and were studied intensively. Three patients were given the drug orally for 6 weeks while the other 5 were treated topically. Oral doses started at 1 mg. a day and were gradually increased to 9 mg. a day. The patients' progress was checked once or twice a week and serum potassium and sodium determinations were made weekly. When a dose of 4 mg. per day was attained, evidence of potassium depletion appeared. When the dose was increased to 9 mg. a day, the depletion of potassium was so severe that it could not be reversed by the oral administration of 12 to 16 Gm. of potassium chloride; the patients also showed evidence of sodium retention and a mild increase in blood pressure. Although the dermatitis showed from 50 to 75 per cent improvement with oral 9-α-fluorohydrocortisone acetate, its use had to be discontinued because of the severe side effects. These same patients were then treated with 9-α-fluorohydrocortisone topically in a 0.1 per cent or 0.2 per cent lotion or ointment. They continued to maintain their improvement over the succeeding weeks and lost their signs of sodium retention and potassium depletion, even though the ointment was applied thrice daily over large areas of skin.

The other 5 patients with atopic dermatitis were given 9-α-fluorohydrocortisone topically for 6 or 8 weeks. They improved rapidly, usually within the first 24 or 48 hours following institution of therapy. The amount of improvement ranged from 50 to 75 per cent and lasted as long as the patient was maintained on treatment. No systemic side reactions resulted from the topical preparations. Relapses usually occurred within 5 to 7 days following cessation of therapy.

The addition of neomycin or gramicidin to the topical preparations of 9-α-fluorohydrocortisone seemed to enhance their effectiveness, even when secondary bacterial factors were not apparent. The 9-α-fluorocortisone was effective in the same type of conditions as hydrocortisone ointment, except that it was effective in lower concentrations. R. W.

Erythema Multiforme Bullosa (Stevens-Johnson Syndrome). Some Observations on Pathogenesis and on Treatment With Cortisone and ACTH. Librach, M. B.: Postgrad. Med. **31**: 570, 1955.

Three cases of erythema multiforme treated with ACTH or cortisone were studied. The first patient, a 4½-year-old child, developed symptoms 8 weeks after he had received sulfonamides, during which a fleeting rash developed, and one week following the administration of penicillin for an upper respiratory infection. His rash and general symptomatology cleared promptly following the administration of ACTH. The second patient, a 24-year-old woman, developed erythema multiforme bullosa after she had been taking phenobarbitone and sodium hydantoinate for one month. There was no complicating infection and she responded promptly to ACTH. The third patient, a 53-year-old man, developed erythema multiforme bullosa after taking Dover's powder,

Benadryl, and aspirin for an upper respiratory infection. His lesions became secondarily infected and failed to respond to penicillin therapy. He was, therefore, given ACTH intramuscularly. Although his temperature subsided promptly, the toxemia and rash increased in intensity and he died a week later. The evidence in favor of an abnormal antigen-antibody reaction as the etiologic factors in these cases is discussed. The pathogenesis of the syndrome and the mechanism of the action of ACTH and cortisone are also discussed. It was concluded that cortisone acts by antagonizing the depolymerization of the mucopolysaccharides in connective tissue resulting from the abnormal antigen-antibody reaction. E. W.

Contact Dermatitis From Selenium Sulfide Shampoo. Eisenberg, B. C.: Arch. Dermat. **72**: 71, 1955.

Three patients developed a contact dermatitis on the ear lobes and in the external auditory canals following the use of a shampoo containing selenium sulfide. Each of the patients had been applying the shampoo for at least 2 months. One patient, who had been using it for 6 months. developed the dermatitis after 3 months of use. When carefully questioned, the individuals remembered that the eruption flared following the use of Selsun shampoo. A patch test of diluted selenium sulfide applied to the area of previously involved skin produced a positive response. By properly plugging the ear canals with cotton before shampooing and then carefully cleansing off the ear lobes with a mild soap immediately after shampooing, each of the patients was able to continue using the preparation. The author calls attention to the fact that, although selenium sulfide shampoo is usually a safe and highly efficient preparation for long-term control of seborrheic dermatitis of the scalp, it is capable, in occasional instances, of sensitizing the neck and ear areas, causing contact dermatitis. R. W.

Miscellaneous Allergies

A Study of the Inheritance of Atopic Hypersensitivity in Man. Tips, R. L.: Am. J. Human Genet. **6**: 328, 1954.

A statistical survey was made of the incidence of atopic hypersensitivity in a large university housing project. An individual was regarded as being atopic if the diagnosis of hay fever, asthma, or eczema was made by a physician at any time during the life of the subject. A survey sample of 99 pairs (husband and wife) was selected for analysis on the basis of residence in the midwestern area of the United States for the last ten years and on the basis of the probability that these members represented a random sample of the population in panmixia of this area.

Of the 198 individuals in this random sample, 20 per cent were classified as atopic. A history of hay fever was present in 16 per cent, of asthma in 7 per cent, and of eczema in 2.5 per cent of the entire group. There was a random association of sex and atopy or the various forms of atopy. Assuming that the predisposition to atopy is governed by a recessive gene and the normal state by its dominant allele, the allele frequencies were calculated for atopy in general and separately for each of the three forms of atopy in this group.

Family histories of atopy for pooled mating analysis were obtained from college students and those residents of the housing project not included in the survey sample. Histories were obtained from atopic individuals and from nonatopic individuals in whose immediate family atopy was present. Only members of the immediate family were included in the history. The basis for selection of family histories for use in pooled mating data analysis was the

same as for the survey sample. The parents in this group ranged from 45 to 60 years of age and the children from 12 to 30 years of age. Children under 12 years of age were omitted from analysis in this group.

The family histories for general atopy and for each trait were classified according to the types of mating—dominant to dominant, dominant to recessive, or recessive to recessive. The proportion of these mating types for hay fever, asthma, and eczema corresponded to the proportion predicted on the basis of the allele frequencies calculated from the survey sample. An analysis of the random normal to hay fever, asthma, and eczema matings for the proportion of recessive children supported the recessive gene hypothesis for these illnesses. An analysis of heterozygote (normal) matings for these individual traits revealed a close correlation between observed and expected numbers of recessive offspring. These observations support the hypothesis that three recessive alleles, each a member of a separate gene pair, govern the predisposition to sites affected in atopic individuals. Predisposition to hay fever is governed by a recessive allele of one gene pair, to asthma by a recessive allele of a second gene pair, and to eczema by a recessive allele of a third gene pair. The data on atopy in general, especially the pooled mating data, failed to support the single recessive gene hypothesis. B. S.

Fatal Hypersensitivtiy to PAS and Streptomycin. Hansen, J. E., and Cleve, E. A.: Dis. Chest **28**: 577, 1955.

A 22-year-old Negro with pulmonary tuberculosis and a negative personal and family history of allergy received PAS in doses of 3 grams 4 times daily for approximately 2 weeks and 1 gram of streptomycin intramuscularly every third day for the same period of time. At this time the patient developed a high fever and a pruritic maculopapular eruption which, within three days, covered the entire body. Review of his record revealed that a rise in temperature had occurred every 3 days, shortly after each injection of streptomycin. This drug, therefore, was discontinued, but shortly thereafter he developed severe conjunctivitis, lymphadenopathy, anorexia, a hacking cough, and a fever of 105° F. PAS was discontinued and he was given large doses of Pyribenzamine. Laboratory studies at this time showed numerous granular and hyaline casts and a leukocytosis, but no eosinophilia. Within ten days all these symptoms had subsided. Ten days later when PAS treatment was reinstituted in the same dosage, the patients temperature rose to 104° F.; he became stuporous and developed a mild recurrence of the skin eruption. He was treated with daily injections of aqueous procaine penicillin. Three days after the onset of this second recurrence, the patient received 1 gram of dihydrostreptomycin intramuscularly. Three hours later he began to experience severe pruritus of the genitalia. All medication was discontinued. He developed a pleural friction rub and an eosinophilia of 23 per cent. Following a convulsive seizure, the patient expired. At autopsy, there was microscopic evidence of tuberculosis in the lungs, pericardium, and spleen, as well as in the cervical, hilar, and mesenteric lymph nodes. The liver was found to be mottled and yellow-brown. Microscopic examination of this organ revealed widespread patches of hepatic necrosis. The kidneys showed evidence of chronic pyelonephritis. It was thought that this case represented a hypersensitivity reaction to PAS and streptomycin. E. W.

Agranulocytosis Complicating PAS and Streptomycin Therapy. Mahrer, R. A., and Maret, R.: U. S. Armed Forces M. J. **6**: 1193, 1955.

Agranulocytosis was observed in a 39-year-old woman following treatment with streptomycin and PAS for tuberculosis. This patient had had a

wedge resection of the left lower lobe for removal of a granuloma consistent with tuberculosis about two months prior, at which time she had received Isoniazid and streptomycin. Streptomycin and Isoniazid were then discontinued postoperatively because acid-fast bacilli were not seen in the excised lesion. However, when Mycobacterium tuberculosis was reported on culture from the excised material about 6 weeks postoperatively, she was given 2 grams of streptomycin every 3 days and PAS in 12-gram doses daily. Within a short period of time she became acutely ill with a fever of 103° F., pulse of 116, respirations of 20, and a red pharynx without ulceration. Laboratory examination of the blood revealed a white count of 700 per c. mm. with a differential of 12 per cent neutrophils, 84 per cent lymphocytes, 1 per cent monocytes. and 3 per cent eosinophils. The hemoglobin and red count were within normal limits. Treatment with PAS and streptomycin was discontinued. The patient was then given 1.2 million units of penicillin, 20 mg. of ACTH, and 200 mg. of cortisone daily. Five days later there was dramatic improvement in her general condition; within a period of about 2 weeks, her white count returned to the normal level. During this time, the ACTH and penicillin were discontinued and the cortisone was gradually reduced until, within 3 weeks, its use had been discontinued. PAS sensitivity was suspected in this case because the drop in the leukocyte count did not occur until this drug was added to the therapy. E. W.

Hepatitis Following Isoniazid. Gellis, S. N., and Murphy, R. V.: Dis. Chest. **28**: 462, 1955.

A 30-year-old white male with pulmonary tuberculosis developed an urticarial eruption with severe pruritus and fever approximately one month after the beginning of streptomcycin and para-aminosalicylic acid therapy. When dihydrostreptomycin was substituted for streptomycin, he developed the same reaction within one hour. Dihydrostreptomycin and para-aminosalicylic therapy was therefore discontinued and the patient was put on 300 milligrams of Isoniazid daily. Nine days after this therapy was instituted he developed icterus, generalized pruritus, and clay-colored stools. X-ray study of the gall bladder was normal. The jaundice subsided within one month and was attributed to hepatitis from Isoniazid. E. W.

Accidents in the Course of Heparin Therapy: Reactions of Allergic Type. Massone, G.: Minerva ginec. **7**: 491, 1955 (Abstract, J. A. M. A. **159**: 1249, 1955).

Allergic reactions to the intravenous administration of heparin developed in several patients who were being treated for thrombophlebitis. One patient who had received heparin therapy for five days without ill effect suddenly developed an allergic shock reaction characterized initially by nausea, sweating, and dyspnea, followed by bronchospasm, cyanosis, and shock. The patient survived. The author classified this reaction as an acquired sensitivity rather than as a primary hypersensitiveness which occurs less commonly and initially produces milder symptoms that become more severe following subsequent injections. M. C.

The Symptoms, Diagnosis and Treatment of Polyarteritis. Lovell, R. R., and Rose, G. A.: Postgrad. Med. **31**: 382, 1955.

Polyarteritis is a disease characterized pathologically by necrosis and inflammation of small- or medium-sized arteries. Clinically, it produces a con-

stitutional illness associated with local symptoms that result mainly from arterial occlusion. Many patients who develop the disease are already suffering from chronic respiratory infections, acute respiratory infections, or rheumatoid arthritis. Early symptoms commonly include fever, tachycardia, weight loss, diffuse aching, and tenderness of the muscles. Later, severe cachexia, an increased erythrocyte sedimentation rate, hypoplastic anemia from marrow hypoplasia or gastrointestinal hemorrhage, neutrophilia, and some degree of eosinophilia are quite common, especially in cases with lung involvement. Most patients have abnormalities of the plasma proteins; the globulin tends to be high and the albumin low. Local manifestations of polyarteritis depend on the tissue or organs involved. The kidney is frequently involved and is the key organ in prognosis, since renal lesions are the commonest cause of death and spontaneous remission is extremely rare. There are two types of renal lesion—renal polyarteritis and a characteristic form of glomerulitis. Renal polyarteritis tends to produce cortical infarcts and is associated with the presence of protein and red cells in the urine, as well as granular and hyaline casts. The clinical picture of this glomerulitis is that ordinarily seen in glomerulonephritis, in either the acute or chronic stage. Cardiac involvement consists of polyarteritis of the coronary arteries and usually manifests itself clinically by cardiac enlargement and congestive failure. At necropsy it is not uncommon to find numerous infarcts, which are usually small. The chief symptoms of involvement of the alimentary canal are abdominal pain, vomiting, diarrhea, and hemorrhage. Polyarteritis of the nervous system, manifested by involvement of the vasa nervorum, shows a characteristic clinical picture of scattered peripheral asymmetrical polyneuritis. The appearance of cutaneous polyarteritis depends upon the depth and size of the affected arteries. Involvement of subcutaneous arteries produces nodules with normal overlying skin. More commonly seen are superficially placed papules which appear in crops, usually on the limbs and especially around the ankles. Infarction of the dermis often leads to hemorrhage, vesiculation, and central necrosis; the consequent ulcers may enlarge to a diameter of several centimeters. A characteristic feature of cutaneous polyarteritis is the development of a purplish reticulation of the skin; usually this appears where there have first been papules, but sometimes it is the first clinical manifestation. Joint manifestations, which are common, are of two types: an acute, transient, migrating arthritis or a more chronic and deforming lesion which resembles rheumatoid disease. In most cases of polyarteritis the lungs are spared. When pulmonary lesions do occur, they precede polyarteritis in many organs, often by months and sometimes by years. Clinically, they may produce asthma, a bronchitic type of illness, or pneumonic consolidation which does not respond to antibiotic therapy. Resultant lung damage may be considerable and may lead to fibrosis, bronchiectasis, or cavitation. The x-ray pattern is very variable; Loeffler's type infiltration is common and often other infiltrations are mistaken for fibrocaseous tuberculosis. One characteristic of lung involvement is eosinophilia in the sputum. Diagnosis is best established by means of a biopsy, and skin lesions which are new and are not complicated by necrosis or infection make excellent sites. Muscle biopsies are also good pathologic specimens, but it may be necessary to repeat the biopsies several times before a positive diagnosis can be made. In the differential diagnosis of this disease, lupus and other collagen diseases, asthma, acute uncomplicated glomerulonephritis, and malignant hypertension must be ruled out. Treatment consists chiefly of the administration of cortisone or ACTH. Of 8 cases treated for 5 years with steroids, 2 have died, 3 were in remission, and 3 were alive but still required cortisone. Both fatal cases had hypertension and died in the malignant phase. E. W.

Allergic Reactions to Penicillin in Workers in Charge of the Antibiotic's Production. Maffei, R., and Napolitano, L.: Minerva med. **46**: 1785, 1955 (Abstract, J. A. M. A. **159**: 731, 1955).

Allergic hypersensitivity to penicillin occurred in 19 of 156 workers employed in a penicillin factory where they were in close contact with the antibiotic. There were 3 cases of asthma, 14 cases of dermatitis, and 2 cases of angioneurotic edema. Patch and intracutaneous tests with penicillin were used in establishing the diagnosis in these cases. It seemed probable that the asthmatic subjects had become sensitized to penicillin by inhaling it. A relationship was noted between the time of exposure to the antibiotic, usually a minimum of several months, and the onset of allergic symptoms. It was emphasized that exposure of workers to penicillin was an occupational hazard. It was hoped that periodic skin testing with penicillin might detect the onset of sensitivity early enough to allow the transfer of such workers to other departments.

Anaphylaxis

In Vitro Anaphylaxis in the Sensitized Mouse Uterus. Fink, M. A., and Rothluaf, M. V.: Proc. Soc. Exper. Biol. & Med. **90**: 477, 1955.

The authors studied anaphylaxis in the mouse with the Schultz-Dale technique in an attempt to establish the role, if any, of histamine in this phenomenon and to determine the effect of pertussis vaccine on in vitro anaphylaxis in this animal.

Virgin female Swiss mice were used for sensitization with alum-precipitated egg albumin. The mice were tested when they were in estrus, at which time the uteri were large. The technical details of the experiments are provided.

The responses of the sensitized uteri to histamine could be blocked in the Dale bath by the previous addition of Benadryl. Similarly, the addition of atropine prevented responses to acetylcholine. These drugs, however, would not prevent or diminish the anaphylactic responses of the uteri to the antigen. In this way it was again demonstrated that neither histamine nor acetylcholine played a major role in mouse anaphylaxis.

In the intact mouse, pretreatment with pertussis vaccine is known to increase both histamine and anaphylactic responses. No such effects could be demonstrated in the isolated tissue experiments. The anaphylactic sensitivity of the uterine horns to the egg white antigen was not increased in the sensitive animals prepared with pertussis vaccine. The increase in responsiveness to histamine was as great in animals prepared with antigen alone as in those receiving antigen plus pertussis organisms. This finding lacks a ready explanation.

Following in vitro anaphylaxis, no perceptible morphologic changes were found in the uterine mast cells, which are believed to be the cells involved in the release of histamine.

Pharmacology, Physiology, and Pathology

Disturbance of Pregnancy in Mouse and Rat by Systemic Antihistaminic Treatment. Shelesnyak, M. C., and Davies, A. M.: Proc. Soc. Exper. Biol. & Med. **89**: 629, 1955.

Ninety female albino mice were placed in cages with fertile males for a ten-day period. During this period, 45 of the females were given daily subcutaneous injections of 1 mg. of Benadryl and 45 were given saline. Normal

pregnancies developed in 6 of the 45 antihistamine-treated animals and in 24 of the 45 control mice. In another series, 100 female mice were housed with males for a period of 5 days. Fifty of the females were then treated with 6 daily subcutaneous injections of 1 mg. of Benadryl and 50 were treated with saline. Three of the 50 antihistamine-treated mice became pregnant, as compared with 10 of 50 controls.

Further studies were done on impregnated albino rats to determine at which stage of gestation the antihistamine interfered with pregnancy. Subcutaneous injections of 15 mg. of Pyrrolazote or saline were given twice daily for 3 successive days to groups of rats from the fourth to the tenth day after coition. The action of the antihistaminic in interfering with pregnancy was most profound when given from the fifth to the tenth day after coition. From 0 to 40 per cent of the rats in the various groups treated with antihistamine during this period remained pregnant, whereas 100 per cent of control animals had a normal pregnancy. The uteri from similarly treated rats were removed from the eighth through the fifteenth day of pregnancy and examined. All uteri showed evidence of fetal absorption and abortion. With one exception all uteri showed that implantation had occurred, but there was subsequent interference with fetal development. It had been shown previously that an artificial decidual reaction can be inhibited by instilling the antihistamine directly into the uterus. The failure of systemic antihistamines to prevent implantation in the above studies is explained by the failure of an adequate amount of the drug to reach the uterus. However, the amount was sufficient to damage the developing fetus. B. S.

Capillary Stress Response and Species. Kramar, J., Meyers, W. V., and Welhelmj, C. M., Jr.: Proc. Soc. Exper. Biol. & Med. **89**: 528, 1955.

The immediate and late capillary response to 8 different forms of stress was studied in guinea pigs, rabbits, and dogs. Capillary resistance was measured by the negative pressure method. Measurements were taken prior to the stress and one-half, one, two, and four hours later (immediate response) and then daily for one week (late response). The immediate response in dogs was either increased or unchanged capillary resistance, regardless of the form of stress applied. The late response in dogs was predominantly that of elevated resistance, but an occasional animal either did not change or showed a decreased resistance or a biphasic response. In guinea pigs and rabbits the immediate and late responses were either increased or decreased capillary resistance or a biphasic reaction, regardless of the type of stress utilized. Previous observations on rats and human beings revealed a similar multiplicity of capillary reactions to various forms of stress. Thus, any species is capable of producing all patterns in capillary response, yet in each species certain patterns predominate. These varied types of capillary response to stress must be taken into consideration in any experimental or clinical study in which capillary resistance is measured. B. S.

Comparative Behavior of I^{131} and C^{14} Labelled Albumin in Plasma of Man. Masouredis, S. P., and Beeckmans, M. L.: Proc. Soc. Exper. Biol. & Med. **89**: 398, 1955.

Two patients were given 100 μc of glycine 2-C^{14} intravenously and 20 to 30 days later about 100 μc of I^{131} human serum albumin intravenously. C^{14} was rapidly incorporated into circulating albumin following the intravenous injection of glycine 2-C^{14} in man. Serial sampling of the plasma for C^{14} and I^{131} albumin was carried out for 60 days. I^{131} albumin was found to leave the

plasma at a rate that was more than twice as fast as the C^{14} labelled albumin. The evidence available suggests that one of the factors responsible for the difference noted is an alteration in the metabolic behavior of albumin brought about by the introduction of I^{131}. Results of metabolic studies based on I^{131} trace-iodinated proteins should be accepted with caution until more definitive data are available. B. S.

Binding of Histamine In Vitro and Its Inhibition by Cortisone. Schayer, R. W., Davis, K. J., and Smiley, R. L.: Am. J. Physiol. **182**: 54, 1955.

The skin of rats pretreated with cortisone loses a significant degree of its ability to bind exogenous histamine in vitro. No such loss of histamine-binding activity was noted after pretreatment with antihistamines, ACTH, DCA, d-catechin, or aminoguanidine. When the skin of the animals was depleted of histamine by the prior injection of 48-80 (a powerful histamine-release agent), the skin was able to bind up to 6 times as much histamine as normal skin. Adrenalectomy also increased the histamine-binding activity of the skin. These experiments indicate that this effect is not brought about by a disruption of the histamine-binding mechanism, but is due to actual prevention of histamine formation. They suggest further that the site where histamine is bound is inseparable from the site where histidine is carboxylated and that an exogenous histamine molecule can enter directly into the unoccupied binding positions. H. F.

In Vitro Influence of Bacterial Pyrogens on Adrenocortical Function of Perfused Calf Adrenals. Rosenfeld, G.: Am. J. Physiol. **182**: 57, 1955.

Pyrogenic bacterial polysaccharides isolated from 3 immunologically distinct bacteria and dissolved in homologous whole blood were shown by in vitro perfusion experiments to have a significant inhibitory effect on the corticoid output of ACTH-stimulated calf adrenals. This depressing effect was also observed when the adrenals were perfused without added corticotrophin. When the pyrogenic material was dissolved in an artificial medium instead of in whole blood, there was no significant effect on the corticoid output of the perfused adrenals. This suggests that there is some intermediary reaction between the bacterial pyrogens and certain of the blood constituents. H. F.

Miscellaneous

Penicillin V, a New Type of Penicillin: Preliminary Clinical and Laboratory Observations. Martin, W. J., Nichols, D. R., and Heilman, F. R.: Proc. Staff Meet., Mayo Clin. **30**: 467, 1955.

Penicillin V was administered orally in various dosages to adult patients and its concentration in the serum was determined at intervals. Since penicillin V is a stable, free acid and is not inactivated by gastric acid, it was given at regular intervals without regard to the degree of gastric filling. In some experiments, comparisons were made with penicillin G administered under similar conditions.

Following a single oral dose of 200,000 units of penicillin V, the concentration of antibiotic in the serum of different patients ranged between 0.175 and 1.32 units per milliliter. With penicillin G, the levels were generally lower, ranging between 0.15 and 0.59 unit per milliliter. After 6 hours, some penicillin V was still present in the blood, whereas penicillin G had nearly always disappeared. With an initial dose of 400,000 units of penicillin V, followed by 200,000 units every 4 hours, a serum concentration of approximately 1.2

units per milliliter was attained in most patients initially, with some decrease in concentration after 26 and 50 hours of treatment. When 400,000 units of penicillin V was given every 4 hours, higher serum levels were obtained than with previous schedules. The serum concentration varied between 1.63 and 4.4 units per milliliter in most patients, although in several instances the concentrations were less than 1.0 unit per milliliter. The authors recommend that penicillin V be administered at intervals not exceeding 4 hours and state that 400,000 units produce more adequate serum levels than lesser dosages.

Tests of sensitivity to penicillin V and penicillin G were carried out on blood agar plates and by the cup-plate methods. *M. pyogenes, Sarcina lutea,* and several other bacteria were used in these studies. Results of these tests indicated that penicillin V has an antibacterial effect similar to that of penicillin G. A clinical study was undertaken in a group of 30 patients with various infections, including acute pharyngitis, acute tonsillitis, acute tracheobronchitis, pneumonitis, pneumonia, acute otitis media, acute parotitis, furunculosis, acute cystitis, cholecystitis, acute infectious arthritis, and peritonsillar abscess. The dosage of penicillin V ranged between 200,000 and 800,000 units every 4 hours. The clinical results were satisfactory in almost every instance. In the more severe infections, reliance was not placed on oral penicillin V alone. Abdominal cramps, diarrhea, and aphthous stomatitis were the only untoward reactions encountered. The results of these preliminary studies indicated that oral penicillin V is an effective therapeutic agent for the treatment of certain infectious diseases. M. C.

The Treatment of Pulmonary Emphysema and of Diffuse Pulmonary Fibrosis With Nebulized Bronchodilators and Intermittent Positive Pressure Breathing. Miller, R. D., Fowler, W. S., and Helmholz, H. F. Jr.: Dis. Chest **28**: 309, 1955.

Twenty-two patients with pulmonary emphysema, 11 of whom were known to have chronic bronchial asthma, were treated for 2 weeks with oxygen administered by intermittent positive pressure breathing 4 times daily for 20 minutes. No improvement was noted subjectively or objectively, as determined by vital capacity and arterial oxygen saturation studies. Forty-three patients received combined treatment as part of three different programs. Thirteen of these patients were known to have bronchial asthma. Ten patients in this group, who had received oxygen by intermittent positive pressure previously, were treated with Isuprel and oxygen with intermittent positive pressure for a 10-day period. Significant symptomatic improvement was noted in 7 of these patients. Similarly, 7 of 10 patients treated with Isuprel and oxygen with intermittent positive pressure were subjectively improved, despite the fact that they had received no previous treatment with oxygen by intermittent positive pressure. Of 23 patients who were treated with oxygen and Isuprel aerosol without intermittent positive pressure for 2 weeks, 18 (or 70 per cent) reported subjective improvement. Twenty-two of this group who had received the Isuprel-oxygen treatment without positive pressure were then treated in the same manner with positive pressure. Fifteen maintained the improvement; 3 became worse. Persistent objective improvement in vital capacity, maximal breathing capacity, nitrogen washout index, or arterial oxygen saturation was unusual. Only 4 of the 43 patients who at some time during the study received the combined treatment had persistent improvement in vital capacity and maximal breathing capacity. Three of these patients were among the youngest tested, namely, 25, 30, and 36 years of age, respectively. In the course of this study, it was noted that many patients who had previously used aerosol bronchodilators were found to be using them inefficiently and incorrectly. When

they were instructed in the correct use of a nebulizer and when they followed a systematic program similar to that used with intermittent positive pressure in combination with aerosol bronchodilators, the incidence of symptomatic improvement was similar to that of patients using the combined treatment during short-term treatment. The lack of persistent change in the results obtained by various tests for pulmonary function suggests that none of these therapeutic methods alter the basic pulmonary lesion. The occasional improvement in arterial oxygen saturation, the decrease in cough and volume of sputum, and the improved sense of well-being would seem to indicate an improvement in the bronchial hygiene brought about by the use of aerosol bronchodilators.

E. W.

Respiratory Disease Research. Dingle, J. H.: U. S. Armed Forces M. J. **6**: 1249, 1955.

A brief review is presented of the respiratory disease research carried on in the Armed Forces and reported by the Commission on Acute Respiratory Diseases. This report covers the period from 1940 to 1954. During this time a new disease entity, namely, acute respiratory disease (ARD), was described. This entity was different from the common cold, from influenza, and from atypical viral pneumonia. It occurred in epidemics among recruits during the winter months, shortly after these men had been assigned to the Replacement Training Center. In most years, seasoned troops were relatively immune to this disease. It was manifested by a short course of mild respiratory symptoms. These included mild fever, chilliness, and headache, accompanied by malaise, anorexia, and symptoms of nasal involvement with a sore throat. Mild hoarseness and cough were frequently encountered. Only rarely did the patients appear to be moderately or severely ill. Physical findings were few and rarely of intense degree. Nasal obstruction, mild injection of the pharynx and palate, and lymphoid hyperplasia on the pharyngeal wall were most frequently found. The febrile course was short, from 2 to 4 days, and the average maximum fever was about 101° F. Constitutional symptoms subsided with defervescence, but symptoms referable to the respiratory tract, when present, tended to persist from 1 to 2 weeks. Leukocyte counts were within normal limits. Recent investigation by Hilleman in volunteer studies proved that virus RI-67 is responsible for ARD. Further studies have proved that following infection with this virus there is an increase in antibody titer for the virus. Investigation into the preparation of a vaccine with virus RI-67 for ARD is being conducted at the present time.

E. W.

Reactions to Influenza Vaccine. Seal, J. R.: U. S. Armed Forces M. J. 6: 1559, 1955.

Among some 77,000 individuals who were vaccinated with influenza vaccine in the Armed Forces during the fall of 1954, 0.03 to 0.09 per cent suffered reactions of sufficient severity to require hospitalization. The average number of days hospitalized varied from 1.6 to 4.8. Only two allergic reactions were observed. Screening for egg sensitivity had been performed before any of the 77,000 individuals was vaccinated. The two patients who experienced allergic reactions had known that they were egg-sensitive but had denied it. One was admitted to the hospital because of severe urticaria following vaccination and the other had an asthmatic attack and was also hospitalized. The relative incidence of severe side reactions was low. The incidence of minor reactions was rather high and included a swollen arm in 50 to 70 per cent, general malaise in 42 to 70 per cent, fever in 31 to 60 per cent, and headache, chills, nausea, diarrhea, and vomiting in lesser degrees. It may be concluded that vaccination

with influenza vaccine is accompanied by a high percentage of transient, mild local and systemic symptoms with relatively little incapacitation or loss of time from duty. E. W.

Echinococcus Disease in an American Veteran. Zelman, S.: U. S. Armed Forces M. J. **6**: 1800, 1955.

An Echinococcus cyst of the liver was discovered in a 40-year-old laborer, who was admitted to the hospital complaining of epigastric pressure and pain which was worse after meals, occasional nausea and vomiting of more than one year's duration, and a weight loss of 14 pounds. During World War II, while in North Africa, the patient had lived for a period of two months in a barn which had housed sheep. Physical examination revealed a firm, small, tender mass in the epigastrium, extending to the umbilicus, which was considered to be an enlarged left lobe of the liver. Aspiration produced a liter of clear, watery fluid under pressure which, wehn examined, revealed no scolices or hooklets. During the 48 hours after aspiration, the patient developed fever, tachycardia, and leukocytosis. The blood eosinophilia, which had been 1 per cent at the time of aspiration, gradually rose to 15 per cent three days later. Intracutaneous testing with Echinococcus antigen resulted in pronounced immediate and delayed reactions. Blood drawn before the skin test gave a positive complement fixation reaction with Echinococcus antigen. Subsequently, a laparotomy was performed, the cyst was aspirated, partially evacuated of its germinal layer, and its contents were sterilized by injection of 10 per cent Formalin. It was then marsupialized to the peritoneum and packed with gauze. In an attempt to minimize a hypersensitivity reaction to spilled hydatid cyst fluid, 100 mg. of hydrocortisone was administered intravenously at operation before the cyst was opened, and steroid therapy was continued during the next two weeks. The patient's postoperative temperature rose to 102.4° F. on the second and third days and fell to normal in the next two days. Only mild leukocytosis and eosinophilia accompanied this reaction. E. W.

The Effect of Repeated Tuberculin Testing on Post-Vaccination Allergy. A Preliminary Note. Magnus, K., and Edwards, L. B.: Lancet **2**: 643, 1955.

In order to observe the effect of repeated tuberculin testing on the intensity and persistence of BCG postvaccination tuberculin sensitivity, children who had been tested regularly each year following their vaccinations were studied and compared with youngsters who were tested for the first time several years following their vaccination. All the testing was done intracutaneously with 10 T.U. of PPD which contained 0.0002 mg. per 0.1 ml. When 10 youngsters in one group were retested for the first time 3 or 4 years subsequent to vaccination, their tuberculin tests were found to be from 10 to 13 mm. smaller than the average observed in 623 children retested annually for at least 3 years. A similar study on two other groups of youngsters produced essentially the same results, except that the difference in the size of the reactions was somewhat smaller. The consistency of the results obtained in these studies would seem to indicate that repeated tuberculin testing influences the intensity and persistence of post-vaccination tuberculin allergy. R. W.

Antibiotic Reactions Resulting From Antibiotic Therapy With a Discussion of the Use of Prophylactic Antihistamines. Brown, E. B.: Am. Pract. **6**: 1881, 1955.

The widespread and often indiscriminate administration of antibiotics seems certain to result in an increase in allergic reactions to these drugs. Sensitization

may occur following any of the various routes of administration. The allergic reactions may be classified in four groups: (1) immediate reactions, which can be anything from mild urticaria to fatal anaphylaxis; (2) serum sickness type of reactions, which occur from 7 to 28 days after the last injection; (3) eczematous reactions, which are usually a result of frequent contact with the drugs; (4) perivascular and hemolytic reactions. To date, all reported fatal antibiotic reactions have occurred after parenteral penicillin, but orally administered drugs can also produce severe reactions which, with increased use, may become much more frequent and serious. Careful questioning of the patient in order to elicit a history of previous reactions to the drugs is of utmost importance, since a patient who has experienced one reaction, however mild, is more likely to sustain a second one. Skin tests are unreliable and misleading and may themselves be the cause of a severe reaction in a sensitive individual. Combining antihistamines with penicillin in an effort to avoid reactions is of doubtful value and may mask a minor immediate reaction which could otherwise serve as a warning to forestall subsequent injections of the drug. H. F.

The Problem of Pulmonary Insufficiency in Disability Rating: A Critical Evaluation of The Need for a Physiologic Classification. Syner, J. C., and Christianson, C. S.: U. S. Armed Forces M. J. **6**: 625, 1955.

Because of the unreliability of physical examination and chest roentgenography in estimating the status of pulmonary function for disability rating, the use of pulmonary function studies in rating pulmonary disability in the Armed Forces should be considered. Pulmonary studies suggested included vital capacity, residual air, ratio:residual air/total lung volume ×100, maximum breathing capacity, dyspneic index, ventilation equivalent of oxygen, expiratory reserve, inspiratory capacity, total lung volume, and the arterial oxygen saturation. E. W.